may confound the analysis of such imaging data. We also present preliminary results from our novel intrinsic imaging technique that measures neuronal NADH/FP fluorescence modulation due to sensory stimulus of the zebrafish lateral line.This technique will, in future, enable us to visualize acquisition and fine-tuning of responses of developing neural systems in the embryo.

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Synaptic ribbon formation during Xenopus inner ear organogenesis

Marti M. Morales, Elba E. Serrano
New Mexico State University, Las Cruces, NM, USA

Ribbon synapses are specialized presynaptic structures that facilitate the fast release of neurotransmitters. They play an important role in auditory neurotransmission, yet little is known about the formation of afferent synapses and ribbon synapse structures during development of the inner ear (Sobkowicz et al.,1982). We initiated anatomical investigations with the goal of determining where ribbon synapses are formed in *Xenopus laevis* mechanosensory hair cells and to characterize their appearance during inner ear organogenesis. Our preliminary data collected with transmission electron microscopy(TEM) confirms the presence of "ribbon-like" synapses in hair cells of the *X.laevis* sacculus, an inner ear endorgan that serves a dual role of auditory and vestibular sense reception. Ribbon synapses ranging in size (250 to 600 nm) were detected in saccular hair cells of post-metamorphic juvenile animals. Ribbon synapses also were found in the sacculus of stage 56 larvae, a stage where the inner ear has formed endorgans but has yet to reach adult morphology with regard to size and axon and hair cell numbers. We hypothesize that the earliest appearance of synaptic ribbons in development will coincide with the differentiation of hair cells in the saccular epithelia (Quick and Serrano, 2005), and that ribbon synapses will continue to form throughout *X.laevis* life as hair cells continue to differentiate (Diaz et al., 1995). TEM images are currently being collected for younger larval stages. Results of these studies will contribute to understanding of the early onset of hearing and balance in *X.laevis*. Funded by NIH NIDCD(DC03292) to EES. MMM is an NIGMS RISE trainee.

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GLI3 and Sonic hedgehog regulate hair cell formation and auditory function in mice and humans

E.C. Driver [1], S.P. Pryor [2], P. Hill [3], J. Turner [4], U. Rüther [3], L.G. Biesecker [4], J. Griffith [2], M.W. Kelley [1]
[1] *NIDCD, NIH, Bethesda, MD, USA*
[2] *NIDCD, NIH, Rockville, MD, USA*
[3] *Heinrich-Heine University, Düsseldorf, Germany*
[4] *NHGRI, NIH, Bethesda, MD, USA*

Mutations in the transcription factor *GLI3*, a downstream effector of Hedgehog (HH) signaling, cause distinct pleiotropic malformation syndromes, including Pallister-Hall syndrome (PHS). PHS is caused by mutations that truncate the GLI3 protein downstream of the DNA-binding domain, mimicking endogenous GLI3 repressor activity. In addition to the previously described features of PHS, we have determined that many PHS individuals also exhibit hearing loss ranging from mild to severe-profound, primarily affecting low frequencies. To determine possible causes of the auditory defect, we examined the inner ears of a mouse model of PHS ($Gli3^{\Delta 699}$). We found that the cochleae of $Gli3^{\Delta 699/\Delta 699}$ mice are significantly shorter and broader than wild-type. On a cellular level, there are further patterning defects, most notably large ectopic patches of hair cells with vestibular rather than cochlear characteristics. As truncated Gli3 represses hedgehog signaling, we also treated cochlear explants with Sonic hedgehog (Shh) to determine the effect of pathway activation on patterning. Consistent with an inhibitory role for Shh in hair cell development, Shh treatment represses development of hair cells in vitro. These findings suggest both a role for hedgehog signaling in development of the cochlear sensory epithelium, and that hearing loss is an important component of PHS. We are further examining Hh signaling in development of the sensory epithelium using conditional alleles of Hh pathway components.

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A transcriptional network controlling male sensory organ development in *C. elegans*

W.H. Chan, S.Y. Yip, A.W. Cheng, K.L. Chow
Hong Kong University of Science and Technology, Hong Kong

Organogenesis requires proper assembly of different cell types. However, the molecular mechanism and developmental regulation governing this process are poorly understood. The nematode *C. elegans* male sensory rays, each composed on only four cells, provide a simple platform for addressing this question. When the assembly of these neuronal and hypodermal cells is defective, ray missing phenotype is displayed. Mutants of *mab-22*, *ceh-43* and *irx-1* all exhibit such phenotype, where all the ray cells are present as documented with cell-specific markers. The feature indicates the abnormality a bona fide assembly defect. *mab-22* encodes a T-box transcription factor and is expressed exclusively in the glial supporting cell. Its expression in the male tail is regulated by at least two evolutionarily conserved transcription factors, *lin-32* and *hlh-2*, the atonal and daughterless homologs, respectively. In addition, *ceh-43* and *irx-1*, homeobox genes of the *Distal-less* class and of *iroquois-class*, are expressed in male tail region. From the genetics studies, *mab-22*, *ceh-43* and *irx-1* mutants can enhance each other's ray missing phenotype synergistically, suggesting that they are acting in a common developmental pathway. Our studies have thus identified